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**Presidente Prof. A. Mussi**

**Tesi di Diploma**

### **MULTISLICE THOMOGRAPHY EVALUATION IN CORONARY ARTERY DISEASE**

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<b>INDEX.....</b>	<b>pg 1</b>
<b>Abbreviations.....</b>	<b>pg 2</b>
<b>Introduction.....</b>	<b>pg 3</b>
<b>History and Fundamentals of MSCT – CA.....</b>	<b>pg 4</b>
<b>Clinical Indication.....</b>	<b>pg 8</b>
<b>Plaque Visualization.....</b>	<b>pg 11</b>
<b>Inclusion Criteria.....</b>	<b>pg 12</b>
<b>Exclusion Criteria.....</b>	<b>pg 12</b>
<b>Our Own Experience.....</b>	<b>pg 13</b>
· <b>Materials and Methods section.....</b>	<b>pg 14</b>
· <b>Inclusion Criteria.....</b>	<b>pg 14</b>
· <b>Exclusion Criteria.....</b>	<b>pg 15</b>
· <b>Patient preparation.....</b>	<b>pg 15</b>
· <b>Scanning and image reconstruction protocol.....</b>	<b>pg 16</b>
· <b>Quantitative Coronary Angiography.....</b>	<b>pg 17</b>
· <b>Image assessment by MSCT.....</b>	<b>pg 18</b>
· <b>Statistical Analysis.....</b>	<b>pg 21</b>
· <b>Results.....</b>	<b>pg</b>
<b>Myocardial Bridges.....</b>	<b>pg 26</b>
<b>Discussion.....</b>	<b>pg 28</b>
<b>Limitation.....</b>	<b>pg 29</b>
<b>Conclusions.....</b>	<b>pg 30</b>
<b>Clinical Cases .....</b>	<b>pg 31</b>
· <b>Clinical Case I.....</b>	<b>pg 31</b>
· <b>Clinical Case II.....</b>	<b>pg 31</b>
· <b>Clinical Case III.....</b>	<b>pg 32</b>
· <b>References.....</b>	<b>pg 33</b>

## **ABBREVIATIONS:**

**ACS = Acute Coronary Syndrome**

**AD = Aortic Dissection**

**CA = Coronary Angiography**

**CABG = Coronary Artery Bypass Graft**

**CAD = Coronary Artery Disease**

**CS = Calcium Score**

**DA = Descending Anterior**

**ECG = Electrocardiogram**

**FN = False Negative**

**FP = False Positive**

**fpVCT = Flat Panel Volume Computed Tomography**

**MPR = Multi Planar Reconstruction**

**MIP = Maximum Intensity Projection**

**CPR = Curved Planar Reconstruction**

**MSCT-CA = Multi-Slice Computed Tomography – Coronary Angiography**

**NPV = Negative Predictive Value**

**PCI = Percutaneous Coronary Interventions**

**PDA = Posterior Descending Artery**

**PE = Pulmonary Embolism**

**PPV = Positive Predictive Value**

**SPECT = Single Photon Emission Computed Tomography**

**TN = True Negative**

**TP = True Positive**

**VR = Volume Rendering**

## Introduction

Conventional Coronary Angiography (CCA) is the diagnostic standard for identification and evaluation of coronary stenosis and coronary artery bypass graft (CABG) patency<sup>1,2</sup>. Limits of this technique (invasivity, undeniable costs, risk of mortality and morbidity) and the large, worldwide, procedure number, whose only one third followed by interventional procedures, because of high percentage of uninjured coronary arteries, suggest the usefulness of a new non-invasive way to visualize the coronaric tree in patients with actual indication to CCA and Percutaneous Coronary Interventions (PCI)<sup>3-6</sup>. Course, dimension and movement are essentially the most complex issues of non invasive coronary imaging. Several studies for evaluating coronaries movement, both their systolic speeds and different "rest" time in diastole, have been carried out <sup>7-9</sup>. To replace conventional CCA, an ideal non-invasive diagnostic imaging technique, because of the mentioned limitations, would need high spatial and temporal resolutions <sup>7,10,11</sup>. The introduction of the first non-invasive system of cardiovascular imaging with an ECG-gated acquisition mode, the electron beam computerized tomography (EBCT), dates back to 1984 <sup>12-16</sup>. In the course of the last decade ongoing, technological research to improve computerized tomography equipments, produced scanner that, from the initial 2 layers, evolved up to arrive at present state-of-the-art: 64 row scanners <sup>7</sup> and more. The first generations of multi-slice computerized tomography (MSCT) used, with 4 layers per "gantry" rotation and a rotation time of about 0.5 s, even if supplied appreciable images, did not allow complete evaluation of the coronaric tree especially in distal segments; images were adulterated from movement artefacts, that prevented from a correct coronaries evaluation <sup>17-18</sup>. On the contrary, the following 16 row scanner generation allowed to assess all coronary segments, halving the length of scanning, from 40 to 20 sec, up to reach less than 12 s by using 40-64 slices equipments. In literature few studies are published about MSCT machine gifted of double source and double

system of detectors. The real advantage of such MSCT scanner is the increase in time resolution, which abolishes, as pointed out by the Authors, the heart rate threshold of 70 b/ min, as necessary inclusion criterion to perform the examination. Trough to the detriment of a higher radiation dose administered to patient, these computerized tomography techniques found their greater field of application in the “triage” of chest pain <sup>19-33</sup> and seemed very useful in “triple rule-out” at the Emergency Department (Runza). This allowed to reduce both cardiac and respiratory movement artefacts and led to consider this technology a good diagnostic method in selected groups of patients, with some important advantages too: non-invasivity, good patient tolerability, non-hospitalization. <sup>34-40</sup>.

The aim of this study is to evaluate MDCT diagnostic performance in identification and quantification of coronary and bypass stenosis, as compared with CCA.

## **History and fundamentals of MSCT technology**

Since introduction, in 1972, of the first generation computerized tomography <sup>41</sup>, for whose discovery, in 1979 Goedfrey Hounsfield and Allan Cormack gained Nobel prize, a lot of technological innovations came out. In past decade, diagnostic evaluation by computerized tomography was an exclusive prerogative of electron beam computerized tomography (EBCT). This equipment was utilized to evaluate myocardial perfusion and cardiac function, and only in a second moment its use was finalized to coronary visualization<sup>42</sup>. EBCT requires 30-40 cranium-caudal transverse sections to evaluate coronaric tree in its full extension. Tomographic slices have a fixed thickness of 3 mm and require an acquisition time of 50-100ms. The heart is visualized during a single episode of 20-30 seconds apnoea. There are some important limitations of performing EBCT: it has an elevated temporal resolution but a low space resolution. Moreover artefacts are common, above all in obese patients. In addition it is impossible to obtain a

retrospective electrocardiographic synchronization, limiting the possibility of rebuilding a predefined<sup>42,43</sup> cardiac phase. In the first nineties, the introduction of spiral CT gave a precious contribution to "not invasive" tridimensional evaluation of big vessels. While in conventional CT gantry executes single rotations at constant intervals along the longitudinal axis (which causes the production of not adjacent scansions, and so a discontinuity in the study of anatomic structures), in spiral CT gantry can perform different rotations around patient without solution of continuity. Moreover, the use of a X-ray tube with a high dispersion of heat allows to obtain a great number of consecutive rotations. Technological evolution also allowed the passage from spiral CT with single detector to spiral multi-detector CT. The first allowed to obtain the acquisition of a single slice for rotation radiogen tube, with space and temporal resolutions that resulted insufficient to examine the heart during a single apnoea<sup>44,45</sup>. Since 1998, multi-detector or multi-slice CT was introduced, that is the most advanced expression of spiral method. It is characterized by small detectors that are overlapped in adjacent slices, in order to obtain more scansions at every gantry rotation. The first multi-detector CT allowed the simultaneous acquisition of 4 slice during a gantry single rotation in a range between 0.5-0.8 seconds<sup>46</sup>. Later 8-16 channels multi-detector CT was introduced, with a minimal gantry rotation of 0.375 seconds. This method allowed an improvement in space resolution, assuring a better signal - to - noise ratio, that is, a fundamental element in image quality, in particular when small structures<sup>43,45</sup> must be visualized.

Moreover, its temporal resolution is significantly lower than electrons beam CT (200-250 ms versus 50-100 ms), though its faster gantry rotation time ( $\leq 0,4$  sec.) and retrospective ECG acquisition assure a good diagnostic accuracy.

The examination protocol includes an acquisition in basal conditions for the quantitative and qualitative evaluation of calcifications (vascular, valvular, parietal and pericardiac). A second administration is implemented after an administration of 120 ml

(4 ml/sec flux) of contrast medium, preceded by the execution of a bolo test of 40 ml of contrast medium in 4 ml/sec flux for the accurate and personalized calculation of the scanning delay.

The most important diagnostic information can be registered after a detailed postprocessing which includes *Volume Rendering* (VR), tridimensional reconstructions, that has a role in understanding anatomy, *Multiplanar Reformat* (MPR) and *Maximum Intensity Projection* (MIP), that are bidimensional reconstruction are necessities in diagnosis, *Curved Planar Reconstruction* (CPR) that allows bidimensional visualization and *Advantage Vessel Analysis* (AVA) protocol, *Navigator*, *Short and Long Axis Reformation and Smart-core*, performed on dedicated *work-station*.

Recently the latest generation of multidetector CT was also introduced, which allows to acquire 64 slices for each rotation simultaneously. The latest generation of MSCT scanners allow the acquisition of 64 sub-millimetric slices for each rotation and enable to reach on a routinary basis, combining an isotropic spatial resolution ( $0,4\text{ mm}^3$ ) and a rotational velocity of 0,33 s, an optimal image quality and the visualization, for instance, of small calibre vassels of the intracranial, pulmonary, mesenteric, renal and periferic district, as well as of the entire coronary tree.

Moreover, in this last area they redefined the MSTC analysis methodology of coronary plaques, allowing to evaluate the internal part of stents<sup>47</sup>.

The insertion of multi-slice systems made possible to acquire a larger body region in the same period of time, with a further improvement in image clarity.

In add to this there is the further advantage represented by a drastically reduction in times of examination performance: an important improvement, considering that for thoracic and cardiac examination patient has to hold inspiratory apnoea to guarantee that image quality is not impaired by thoracic movements.

After all, clinical impact of the new technologies consists of improving image in terms of both spatial and temporal resolution.

The improvement in spatial resolution concerns several aspects of the non-invasive coronary imaging:

- Increases the capability to visualize small calibre vassels (e.g. distal coronary ramifications)<sup>48</sup>;
- Increases the capability to quantify the calcium inside the coronaries;
- Allows to decrease the stent “blooming” effect and therefore it visualizes the intracoronary volume inside the stents;
- Allows to better define the presence of coronary plaques and better quantify their characteristics (e.g. volume, attenuation etc.)

The improvement in the temporal resolution concerns several other aspects of non-invasive coronary imaging:

- Increases the capability to capture the images in a specific time of the cardiac cycle;
- Allows to find additional reconstructing windows inside the cardiac cycle;
- Increases the system performance when the left ventricular function needs to be evaluated;
- Decreases the scanning time.

Recent introduction of the dual-source MDCT has further improved temporal resolution for cardiac imaging. Work in progress on the potential of the dual-energy CT, the 256-slice MDCT, and the flat-panel Volume CT (fp VCT), suggest the possibility of new and interesting cardiac applications<sup>49</sup> because of the reduction of limitations due to cardiac frequency e/o cardiac rhythm. Dual source technology improving temporal (Dual source) and spatial resolution (fpVCT). Flat-panel volume CT scanners can be thought of as conventional multidetector CT scanners in which detector rows have been replaced by an area detector. The flat-panel detector has wide z-axis coverage that enables imaging of entire organs in one axial acquisition. The high-volume coverage and continuous rotation of the detector may enable depiction of dynamic processes such as



coronary blood flow. The contrast resolution of flat-panel volume CT is slightly inferior to that of multidetector CT and a higher radiation dose is needed to achieve a comparable signal-to-noise ratio<sup>50</sup>.

We attend highlights of these new technologies but their radiation dose it appears still high and represent an unjustified biologic cost.

## **clinical Indications**

For a correct patient selection proposed for MSCT coronary angiography, it would be necessary to refer to some guidelines, which nowadays have still not been realized. Real indication to use of MSCT meet controversial opinions of several Authors, but nowadays exist experts consensus statement<sup>51</sup>, that trace the right way to use this technology.

More studied and debated clinical applications with many data in literature concern:

- Patients with atypical thoracic pain and low/intermediate risk of ischemic cardiopathy<sup>51</sup>. These patients, in experience acquired so far, should undergo any way an ergometric test first, as it has been stated in 1997 by the ACC-AHA guidelines for the exercise ECG test. In borderline patients, or with aspecific symptoms, with several cardiovascular risk factors (smoking, hypertension, dyslipidemia, diabetes mellitus, obesity, familiarity) and doubtful or not performable ergometric test, MSCT represents a valid and effective diagnostic alternative<sup>52</sup>. On the contrary, patients with medium/high cardiovascular risk, who are very likely to have a more or less severe coronary pathology, should undergo coronary arteriography, after which a coronary angioplasty might be performed.

- MSCT patients follow-up with previous implant of aortic coronaric by-pass is actually unappropriated. By-pass great diameter allows the evaluation of patency or occlusion with high diagnostic reliability. Sensibility in this event is included between 86-100%, while for specificity values swing between 95-100%<sup>53-58</sup>. It needs to underline that metallic clips very near to by-pass can impede an exact evaluation. By-pass distal anastomosis results often difficult to visualize and the presence of very calcific coronaries prevents from an adequate evaluation.

- About coronaric stent follow-up there are no sufficient evidences except in case in which stents are not positioned in the principal branches and / or great caliber. In fact, literature data indicate that 16 slices CTMS scanners are able to identify stents occlusion or patency that have been previously implanted<sup>59-61</sup>. Moreover proximal or distal stenosis can be found. Using 16 slices CTMS for stents patency evaluation, sensibility and specificity have been respectively reported equal to 78 and 100%<sup>60</sup>. The principal limitations of coronaric stent evaluation by CTMS are due to coronaric movement and “blooming” artefacts, linked to stents material and small diameter<sup>61-63</sup>. The use of “compatible CT” stents, that are constituted of materials without artefacts, could open a new fundamental chapter in CTMS follow-up of angioplastic coronary intervention. Absorbable stents tested in the ABSORBE study that do not leave trace of them are an example.

- Coronaric abnormalities evaluation. The anatomic course of abnormal vessel can be obtained by 3D Volume Rendering rebuildings that evidence also the relationship with other cardiac structure, aorta and pulmonary artery. The coronary anomalies can be a cause of sudden death in the young, such as when a coronary artery courses between aorta and pulmonary artery. This anomaly can be easily diagnosed by using AC-CTMS<sup>65-67</sup>.

- Morfologic and structural study of the heart and in particular of Aortic and Pulmonary Artery disease are specific indications.

An interesting and debated application is the “triple rule – out”: the exclusion of three life-threatening pathologies ( Acute Coronary Syndrome - ACS -; Pulmonary Embolism - PE -; Aortic Dissection – AD ) with one test. Acute myocardial infarction (AMI), PE, and AD are diseases associated with acute chest pain and may lead to severe morbidity and mortality. These diseases may not be trivial to diagnose in the settings of emergency room. ECG-gated multi-detector computed tomography (MDCT), already established for the assessment of pulmonary embolism and aortic dissection, provides reliable information regarding the triage of patients with acute coronary syndrome in the emergency room. MDCT recently appeared to be logistically feasible and a promising comprehensive method for the evaluation of cardiac and non-cardiac chest pain in emergency department patients. The possibility to scan the entire thorax visualizing the thoracic aorta, the pulmonary arteries, and the coronary arteries, could provide a new approach to the triage of acute chest pain.<sup>68</sup>

Quantification of coronaric calcium and characterization of atherosclerotic plaque are two interesting fields in which the role of MSCT has been widely studied in literature.

Some studies proved correlation between quantity of calcium into coronaries and risk of a successive ischemic event, but there is not yet a general consent about the importance of calcium score as a further risk factor, besides the ones falling within the Framingham score for ischemic risk assessment in asymptomatic patients. Calcium Score ( CS) evaluation is feasible and indicate not only plaque place, but also plaque extension.<sup>69</sup> When CS is > 400 there is high probability of coronary stenosis.<sup>70-71</sup> CS seems to have a major role in primary prevention.

## **Plaque Visualization**

CCA is a projective, bidimensional technique that, despite high spatial and temporal resolution, is a luminographic technique with consequent stenosis underestimation. MSCT offers major informations on vessel wall and on its alterations. The Atherosclerotic plaque characterization by MSCT could be particularly important in order to make an accurate diagnosis of ischemic cardiopathy.<sup>72</sup>

Actually, plaque ulceration with subsequent thrombosis represents a dangerous and potentially lethal event.

Rupture risk seems to depend on composition of the same plaque: the most part of ulcerations takes place in adipose plaques, that are formed by a high percent of lipidic components and are covered by a thin fibrotic cap.

Small ulcerations may be asymptomatic at all, while larger lesions are a potential cause of unstable angina, myocardial infarction and sudden death.<sup>72</sup>

Nowadays, intravascular ultrasonography (IVUS) represents the gold standard in plaque characterization. Therefore, by MSCT it is possible to distinguish among soft, fibrotic or calcified plaques<sup>73</sup>, but an effective correlation between atherosclerotic plaque structure and ischemic patient prognosis has still not been proved. MSCT substantially underestimate plaque volume as compared with IVUS.<sup>74</sup> Further improvements in image quality to achieve reliable assessment, especially of noncalcified plaque throughout the coronary tree were evaluated in a post-mortem coronary fpVCT analysis that provided an accurate and reproducible method for the quantitative assessment of both luminal stenosis and atherosclerotic plaque size.<sup>75</sup>

## **Inclusion criteria**

Usually, inclusion criteria to make a scan include:

- Heart rate < 65 bpm (spontaneous or induced by administration of beta – blockers)
- Sinus rhythm
- Capability of holding the breath for a period compatible with scanning Times. <sup>48, 51</sup>

These criteria are necessary to avoid movement artefacts.

As regards heart rate, the problem is the residual movement of coronaric movement in every phase of the cardiac cycle.

Bradycardia allows to stretch diastolic interval and this causes a prolongation of telediastole, during which the heart and the coronary arteries are almost lacking in movement.

Capability of holding the breath is necessary to avoid movement artefacts linked to respiratory movement. Actually, it is evident that patient respiration during scanning considerably reduces quantity and quality of acquired information.

## **Exclusion criteria**

Patients with heart rate  $\geq 75$  bpm, hyperkinetic arrhythmias such as atrial fibrillation, known intolerance to iodinate contrast medium, renal insufficiency (serum creatinine >120 mmol/L), pregnancy, respiratory insufficiency, severe heart failure and all unstable clinical conditions on the whole, are excluded from angiographic study by MSCT.

Several data published in literature show that a high heart rate reduces scan performance and success in terms of diagnostic quality<sup>76-77</sup>.

50 – 200 mg of metoprolol are administered by mouth to all patients who show heart rate > 70 bpm, 45 – 60 min before scanning.

When patient reports to have had a mild or moderate allergic response to iodinate contrast medium, scan is performed after desensibilization by antihistaminic and cortisomic drugs.

In case of renal insufficiency, administration of contrast medium can be better tolerated if an isosmolar drug is chosen <sup>78</sup>.

Respiratory insufficiency and an unstable clinical state can avoid an adequate apnea during scanning.

Patients affected by severe heart failure usually are not able to keep supine position and they usually show high heart rate which, as already said, represents a contraindication to performing an AC – MSCT.

## **OUR OWN EXPERIENCE**

Our study is a performance test carried out to assess the specific capability of MSCT, as compared with coronaric angiography (*gold standard*) to find out significant stenosis in symptomatic patients or in the presence of aorto – coronaric grafts or stents in subjects who already have undergone revascularization interventions.

### **· Materials and methods section**

Since May 2005 up to September 2007 all patients who underwent both AC – MSCT and traditional coronarography were evaluated.

So the enrolled population included 119 patients with atypical thoracic pain or unstable angina. This population was divided into two groups: the first was formed by 83 patients (63 men and 20 women; mean age:  $62.7 \pm 8.3$  years), who were admitted to evaluate their coronaric disease; the second constituted of 36 patients (30 men, 6 women; mean age:  $58 \pm 12$  years), who previously had undergone revascularization by aorto – coronaric by – pass, and in which grafts had to be evaluated. From the first group 33 patients were excluded because of the inability to maintain a correct inspiratory apnea for at least 12 seconds ( $n = 4$ , 4.8%), average heart rate  $> 70$  bpm, with proved failure of  $\beta$  – blocker administration ( $n = 3$ , 3.6%), with creatinine serum levels  $> 2$  mg/dl ( $n = 5$ , 6%) and known intolerance to iodinate contrast medium ( $n = 4$ , 4.8%); subsequently, patient population suitable for the study resulted equal to 50 patients (39 men, 11 women; mean age  $60.9 \pm 9.2$  years). Patients, so selected, after signing an informed consent underwent coronaric angiography by MSCT (MSCT - CA) and then by traditional coronarography. Stent evaluation was performed assessing a subgroup taken from the previous two (18 stents).

· **Inclusion criteria**

Criteria listed below were considered essential to include patients in the study:

- Indication for undergo an elective diagnostic coronarography
- Detection of sinus rhythm by EKG
- Capability of holding the breath for a period compatible with scanning times (13 – 14 seconds)
- Heart rate  $< 65$  bpm
- To have signed an informed consent

- **Exclusion criteria**

The presence of criteria reported below was considered enough to exclude studied subjects:

- Patients in which an effective control of heart rate did not result possible.
- Hyperkinetic arrhythmias (for example, atrial fibrillation, extrasystolia)
- Known intolerance to iodinate contrast medium
- Renal insufficiency (serum creatinine >120 mmol/L);
- Pregnancy
- Unstable clinical conditions
- Acute coronaric syndrome

- **Patient preparation**

100 mg of tartrate metoprolol were administered by mouth to all patients who showed not adequate heart rate, 45-60 min before scanning. Moreover, if considered opportune, a dose of tranquilizer was also administered (1 mg of lorazepam). We never prepare patients with nitrates during this study.



· **Scanning and image reconstruction protocol**

Angiographic scan was performed by a CT 40 detector spiral scanner (Philips Brilliance 40) till February 2006 and by a 64 detector scanner (Philips Brilliance 64) until September 2007.

At the beginning a scanning without contrast medium was carried out, in order to choose interest volume and to visualize eventual coronaric calcifications (*calcium score*).

By using a dedicated software, exact dose of ionizing radiations to which patients had been exposed during the examination was calculated: average value was different according to patient sex if examination was performed by the 40 detector equipment (14 mSv in women and 11,5 mSv in men) while it was equal to 20 mSv by the Brilliance 60 scanner.

Then 100 ml of iodinate contrast medium were administered at a speed of 5 m/s, by an automatic injector linked to 18 – gauge – cannula, which was previously put into the right antecubital vein. To optimize coronaric opaqueness, the *bolus – tracking* approach was chosen, in order to have a synchronization effect between contrast medium injection in coronaric arteries and scanning beginning.

Data from angiographic scan were elaborated after a single 12 – 13 sec. inspiration.

Retrospective reconstructions, based on EKG signal, were made in order to get a high – quality image which was free from movement artefacts as far as possible.

Raw data after every MSCT were reconstructed at different R – R interval percents (from 25% to 70%), so that each coronaric vessel could be visualized in its best phase. Diastolic phase of cardiac cycle was chosen in all patients (70% of the R – R interval).

Reconstruction algorithm collected data coming from a single heart beat, in the course of half radiogenic tube rotation.

So it was possible to reach a temporal resolution of < 210 msec.

· **Quantitative coronaric angiography (QCA)**

Traditional coronaric angiography was performed within 7 days from MSCT examination.

Two in – blind observers analyzed every coronaric segment, dividing coronaries into 16 segments according to the American College criteria; aorto – coronaric grafts were rather divided as follows:

- if venous grafts, into proximal anastomosis, body and distal anastomosis
- if arterial grafts, into body and distal anastomosis

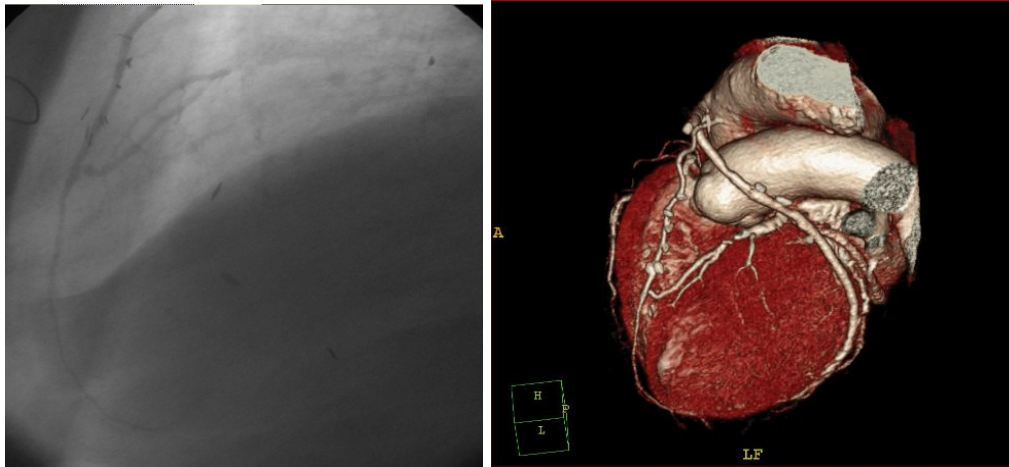
By – pass sequential segments were considered as further single grafts, whose body and distal anastomosis were taken into account.

All segments, without gauge limits, were included in the comparison between MSCT and conventional angiography.

An automatic algorithm to detect vessel border and subsequently to assess coronaries and grafts diameter was applied.

Stenosis were evaluated according to reduction percent as compared with reference diameter, which in turn was calculated in two orthogonal planes, using the average value of the two samples as final value.

Identified segments were classified according to two parameters: as “not significantly sick”, that is, with lumen irregularity or diameter reduction  $< 50\%$ , or as “significantly sick”, if lumen stenosis was  $\geq 50\%$ .



**Fig.1** LIMA to anterior descending artery: conventional angiography and its corresponding angio- CT.

· **Image assessment by MSCT**

After acquiring them, images were sent to a dedicated work station. Single axial images were elaborated again both by a Multi – Planar – Reformat (MPR) two – dimensional reconstruction, which is able to give representations arranged on different planes from that of acquisition, and by three – dimensional Volumetric rendering (VR), which can visualize the heart and the anatomic structures near to it as three – dimensional objects, even adjustable in the space to own liking. In this phase of the study two blinded observers evaluated all patients enrolled in the experimentation.

Images at the highest intensity were used to identify lesions in explored segments, while multiplan images were useful to classify lesions as more or less significant.

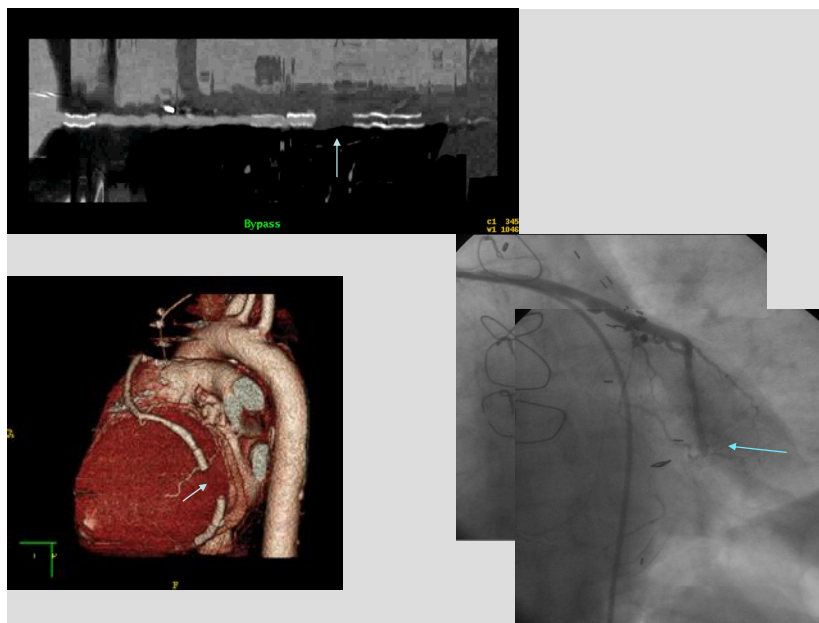
With regard to image quality, it was assessed per segment and classified as follows:

- good, if vessel lumen was perfectly visualized
- adequate, if vessel lumen was well – visualized, through the presence of artefacts

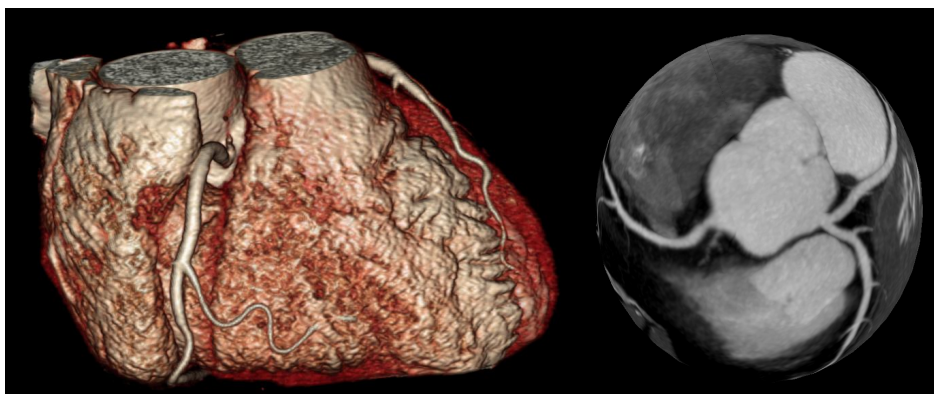
· low, in cases in which vessel lumen resulted scarcely visualized because of the presence of artefacts.

Therefore, stenosis were defined as significant just when they obstructed lumen  $\geq 50\%$ .

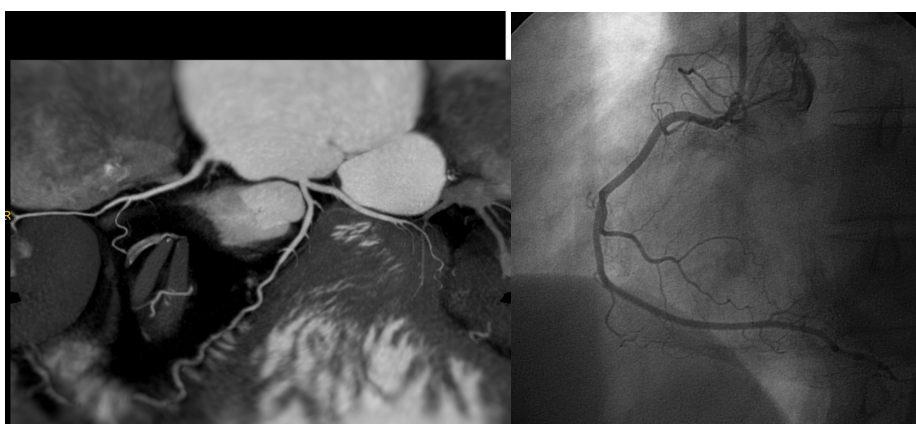
Some cases of beginning disagreement among observatories were evaluated in agreement afterwards.



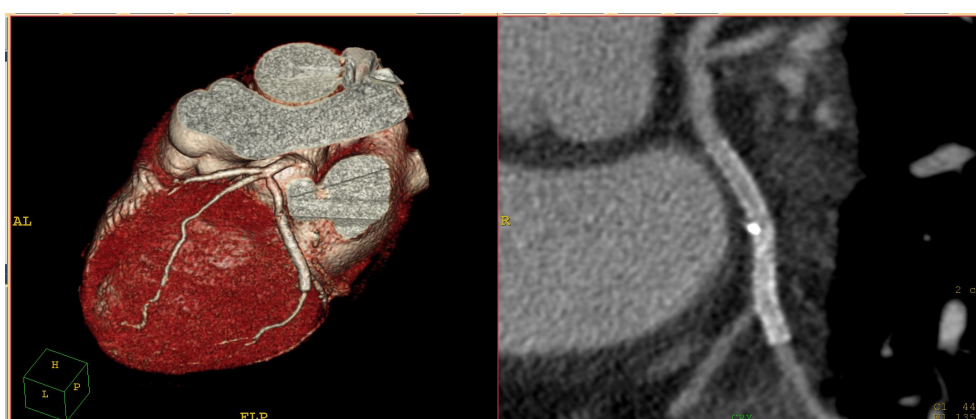
**FIG.2.** *MSTC: Volumetric Rendering (VR) image and multi planar reconstruction of stented saphenous vein graft to seq. obtuse marginal branch – posterior artery.*



**Fig 3.** *Volume Rendering and MPR globe of uninjured coronaries.*



**Fig 4.** *Coronary angio-TC and traditional coronarography.*



**Fig 5.** *Post – stenting Volume Rendering and MPR: failed overlap of 2 stents.*

· **Statistical Analysis**

Data regarding diagnostic accuracy of angiography by MSCT in finding out significant atherosclerotic lesions or significant restenosis, evaluated by using coronaric angiography as reference technique, are reported below in terms of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), with confidence intervals of 95% (tab. 1). CCA vs MSCT-CA comparison has been conducted per segment, per vessel and then per patient. As regards CABG, comparison between conventional coronaric angiography and MSCT was performed assessing every graft, both including body and anastomosis. Intra and inter – observatory variability in identifying significant stenosis was assessed (lumen reduction  $\geq 50\%$ ) and evaluated by Kappa statistic. For statistical analysis we used a dedicated software ( Statistica 5.0, StatSoft Italia, Vigonza – PD )

· **Results**

By a dedicated software has been calculated radiation dose: average value presented sex based difference and resulted 14 mSv for female gender and 11,5 mSv for male with 40 slices technology; average value of 20 mSv with 64 slices.

Average heart rate of the sample was equal to  $59,6 \pm 7,4$  bpm; intra - and inter – observatory variability resulted to be 0,75. Second AHA classification<sup>79</sup>, we considered 17 coronary segments, so potentially we 800 segments were considered. 177 segments don't were visualized during CCA because of Intermedius branch absence or non dominant arteries ( n=130 seg), proximal arterial occlusion with lack of distal branch visualization ( n= 47 seg.). Only 0,8% of total segments ( n=5) non-evaluable because of movement artifacts. Scanning was successful in all patient. Telediastolic phase utilized

in 70% (35/50) of patients, the latter in telesistolic phase because of movement artifacts. An overall number of 618 coronaric segments were evaluated.

92 grafts were evaluated, of which 36 were arterial (26 left and 10 right internal mammary arteries) and 56 were venous; analyzed anastomosis were 102, of which 38 were proximal and 64 distal; explored bodies were 78; 8 venous grafts not evaluated because of the presence of artefacts caused by metal clips.

For the same reason distal anastomosis of an arterial graft was not evaluated, 8 saphenous grafts, 6 left internal mammary arteries and 2 right internal mammary arteries resulted obstructed.

Results concerning diagnostic accuracy for coronaries are reported in table 1, 2 and 3 in tables 4 and 5 are listed data concerning grafts and stents, respectively.

**Tab 1.** *Performance test per segments.*

Segmento		sens	spec	PPV	NPV
RC					
1	Proximal RC	95,2%	96,7%	90,9%	98,3%
2	Middle RC	93,3%	94,6%	82,4%	98,1%
3	distal RC	87,5%	100,0%	100,0%	98,2%
4	PD	92,9%	100,0%	100,0%	96,4%
LM					
5	LM	92,3%	98,6%	92,3%	98,6%
AD					
6	Proximal AD	96,2%	93,0%	86,2%	98,1%
7	Middle AD	85,2%	90,7%	82,1%	92,5%
8	Distal AD	87,5%	100,0%	100,0%	98,5%
9	1° diagonal branch	81,3%	91,8%	76,5%	93,8%
10	2° diagonal branch	83,3%	97,1%	83,3%	97,1%
CX					
11	Proximal CX	91,7%	98,2%	95,7%	96,4%
12	1° marginal branch	100,0%	94,7%	78,6%	100,0%
13	Middle CX	88,9%	95,0%	72,7%	98,3%
14	2° marginal branch	100,0%	97,0%	75,0%	100,0%
15	PL branch	83,3%	96,6%	83,3%	96,6%
RI					
16	IR	100,0%	88,2%	71,4%	100,0%

**Table 2.** *per vessels analysis.*

RC	92,5%	100,0%	100,0%	93,5%
CX	94,4%	95,6%	94,4%	95,6%
AD	95,6%	94,7%	95,6%	94,7%
LM	93,8%	98,5%	93,8%	98,5%



**Tab 3.** Per patient diagnostic accuracy.

<b>n. pts</b>	<b>Sens. (%, n)</b>	<b>Spec. (%, n)</b>	<b>VPP (%, n)</b>	<b>VPN (%, n)</b>	<b>DA (%)</b>	<b>LR+</b>	<b>LR -</b>	<b>Odds pre-test</b>
<b>50</b>	<b>100 (36/36)</b>	<b>100 (14/14)</b>	<b>100 (36/36)</b>	<b>100 (14/14)</b>	<b>100</b>	$\infty$	<b>0.00</b>	<b>1.00</b>

**LR = likelihood ratio; NPV = negative predictive value; PPV = positive predictive value**

	<b>SENS</b>	<b>SPEC</b>	<b>PPV</b>	<b>NPV</b>	<b>DA</b>
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**Tab 4.** *Graft Performance test*

Bodies	100%	94%	80%	100%	95%
Proximal Anastomosis	100%	100%	100%	100%	100%
Distal Anastomosis	75%	96,5%	75%	96%	94%
CABC in toto	94%	92%	88%	96%	93%
Arterial CABG	100%	92%	86%	100%	95%
Venous CABG	90%	93%	90%	93%	92%
OCCLUSION	100%	100%	100%	100%	100%

**Tab 5.***Diagnostic Performance for stents*

	SENSITIVITY	SPECIFICITY	VPP	VPN
STENT	100%	93,3%	80%	100%

## Myocardial bridges

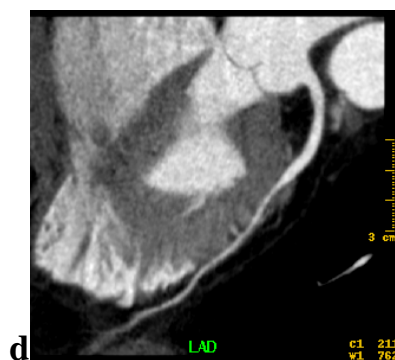
The presence of myocardial bridges represents another interesting aspect of coronaric pathology, of which MSCT shows more clearly anatomic features (fig. 6), resulting very useful for clinical management of this condition and for assessing of its

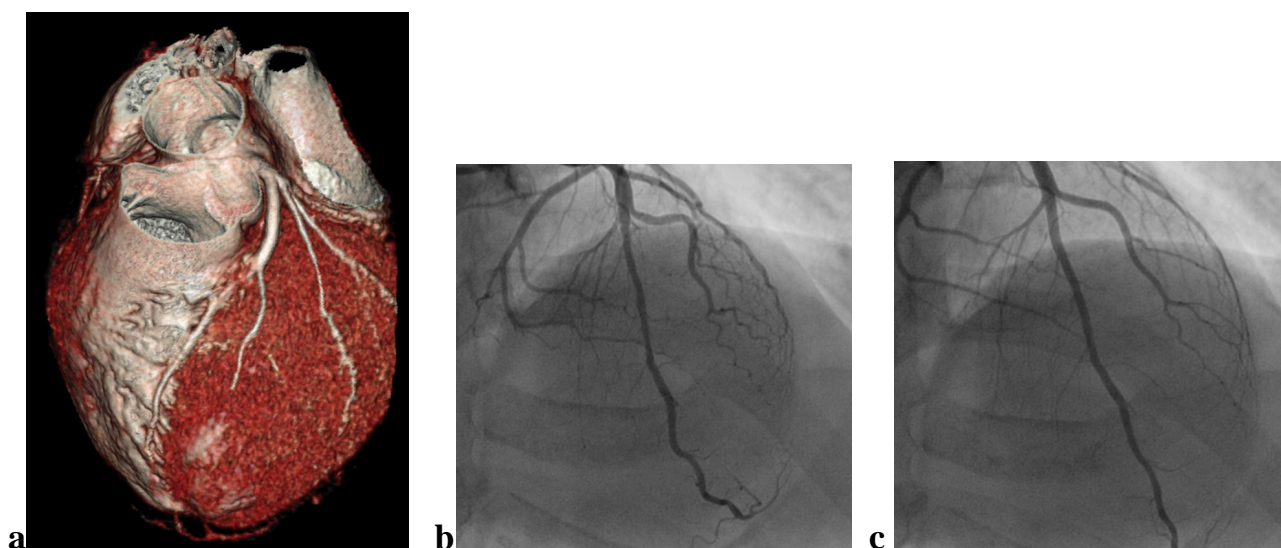
actual incidence in population. Actually, this last is about 0,5 – 12% according to coronaric angiography and 5 – 86% according to necroscopic case studies <sup>80</sup>.

In this study population we observed (86 patients who underwent AC – MSCT and coronarography) 17 bridges/courses (19,8%) were highlighted by CT and only 7 (8,2%) by coronarography.

In all cases the abnormality involved anterior descendent artery, and all bridges were single, 5 of them were symptomatic (as isolated coronaric abnormality) with a deep course.

After their identification, it is possible to choice specific therapeutic options, suggesting “ad hoc” medical treatment.





**Fig 6.** a) VR shows MB in II tract of DA; b)CCA DA systolic squeezing; c) CCA diastolic phase, normal caliber; d)MPR, intramural tract.

## Discussion

Multi-slice computed tomography allows reliable evaluation of the coronary arteries in a non-invasive manner. In general, the high negative predictive value is considered to be the major strength of the technique and a normal MSCT virtually excludes significant CAD on conventional coronary angiography.

CAD is the leading cause of mortality and morbidity in occidental countries; such issues suggests that MSCT based coronary screening, is logic, feasible and careful, but it is today a concept widely refused because of high risk of radiation exposure. On the basis of current literature it is difficult understanding in wich class of patients may be helpful MSCT application. It' s interesting evaluate high risk patients for CAD even if asymptomatic but up to day is ungiustified, while is more acceptable use in patient with dubious exercise test and aspecific symptoms or scheduled for valvular replacement.

Our experience shows good MSCT diagnostic performance when compared to CCA in evaluating CABG patency, in >50% coronary stenoses identification and much more in excluding coronary disease in symptomatic patients and, finally, in detecting other coronary aspects, such as myocardial bridge. Some functional index of perfusion, such as slow-flow phenomenon, that is index of CABG degeneration, is not available with MSCT that seize only morphologic aspects. A good exam execution requires careful patient selection and both pharmacological and technical preparation, then patient education to maintain a correct breath-hold. Major diagnostic difficulties came from coronaric calcifications, that are responsible of modest percentage of false positives. High sensitivity and specificity, PPV and NPV in per segment analysis, that increase in per vessel analysis and raise up to 100% in a per patient evaluation, shows that MSCT is capable in identifying CAD patient that need CCA. Metallic parts such as post-toracotomic suture, metallic clips, valvular prosthesis, electrocatheters, heavily limit images lecture. Consideration on stent evaluation are not feasible in our study because of low prevalence of restenosis in a small sample dimension. Another issue is high radiation dose exposure, that we consider an important limitation and is reason of technical research besides right clinical exam indication. Radiation dose exposure needs ulterior studies and probably may be solved by newer software and scanner introduction. Prospective ECG-gating( i.e.) using a 'step-and-shoot' axial scanning protocol has been shown to reduce radiation exposure effectively while maintaining diagnostic accuracy.<sup>81</sup>

## **Limitations**

The esteemed radiation dose CA-TCMD is more raised than conventional AC. The exposure to ionizing radiations can be reduced with perspective modulation. This technique can reduce the exposure to ionizing radiations of the 50% in patients with low cardiac frequency, but is more sensitive to arrhythmias and limits the possibilities of datasets reconstructions during telediastolic phase. Exist, besides, automatic modulation dose systems (Dose-Right-ACS, Automatic Current Selector, e DOM, Dose Modulation, Philips Medical Systems) that may combine modulation of delivered current both in relation with angular attenuation coefficient of the examined region and through a modulation dose system in Z axis. Referring to initial “scout view”, the milliamperage is automatically modulated along acquisition volume on the basis of angular attenuation coefficient of the examined region and on the basis of attenuation values of tissues along Z axis<sup>82-83</sup>. So an elevated Calcium Score (CS) (i.e. >400) reduces MDCT diagnostic accuracy<sup>38,84</sup>. Severe calcifications, in a single coronaric segment, make impossible lumen evaluation with stenosis overestimation. For this region in our study we evaluated incorrectly a Left Main stenosis (>50%), in a patient with total Calcium Score 1331,8 using Agatston system, of whom 83,4% localized in Left Main. It is important to consider not only total calcium score (i.e. > 400 sec. Agatston) but the calcic distribution in coronaries. In this study, moreover, cardiac and respiratory movements artifacts impaired evaluation capability in 29,4% of coronaric tree, in one patient. Patients collaboration is important in performing correct examination, so this technique up to day is also a patient-dependent exam. Better technology and newer scanner with better temporal resolution such as double source gifted with double detector systems can improve our diagnostic capabilities, diminishing the so called “patient-dependence”.

## **CONCLUSIONS**

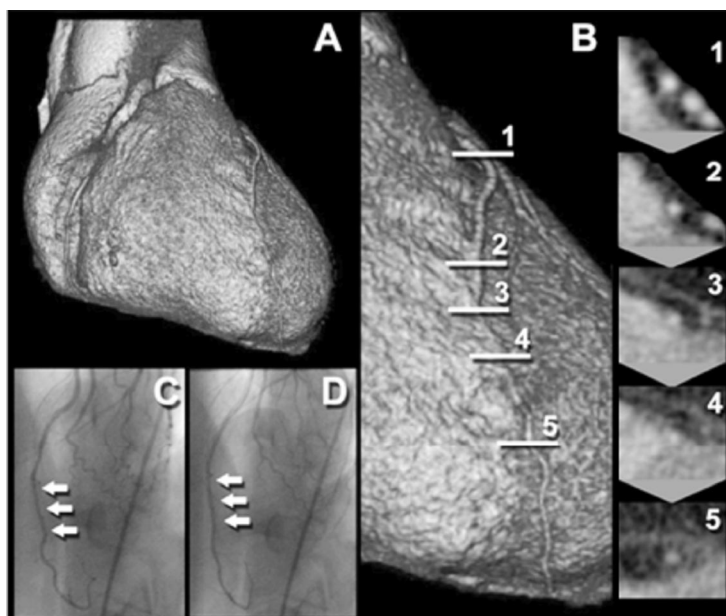
Multi-slice computed tomography (MSCT) is a rapidly developing technique and allows reliable evaluation of the coronary arteries and CABG in a non-invasive manner. Despite limitations due to calcium, movement, metallic parts and high radiation dose, MSCT – CA showed a good diagnostic capability in detecting significant coronary artery stenosis in patient with suspected or known significant coronary artery disease. Moreover, in our experience, is a valuable tool for assessing coronary artery bypass graft patency in patients with clinical suspect of occlusion. It's a good, adjunctive, way to correctly select CCA patient in dubious case. Multiphasic diagnostic approach with new systems of automatic modulation of radiation dose and new algorithms in images reconstruction are fundamental to reduce the important “patient-dependence” threshold. Candidates to MDCT should remain, however, restricted and selected on the basis of patient's balanced diagnostic iter to avoid unjustified risk of ionizing radiation.

### ***Clinical cases***

#### ***Case I***

Female 64 y.o., ipertension, diabetes, referred for chest pain

Dubious exercise test, negative SPECT. MDCT-CA shows healthy coronaries with long myocardial bridge of Descending Anterior artery. (Figure below)



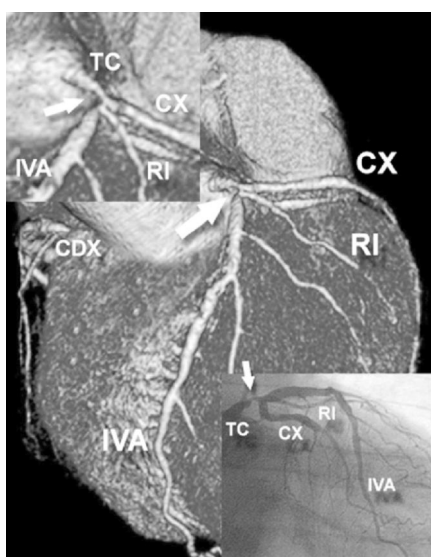
#### **Case I.**

**Image A.** VR; **Im. B.** particular of intramural tract; **Im. C and D,** systolic and diastolic caliber variation due to myocardial squeezing



### Case II

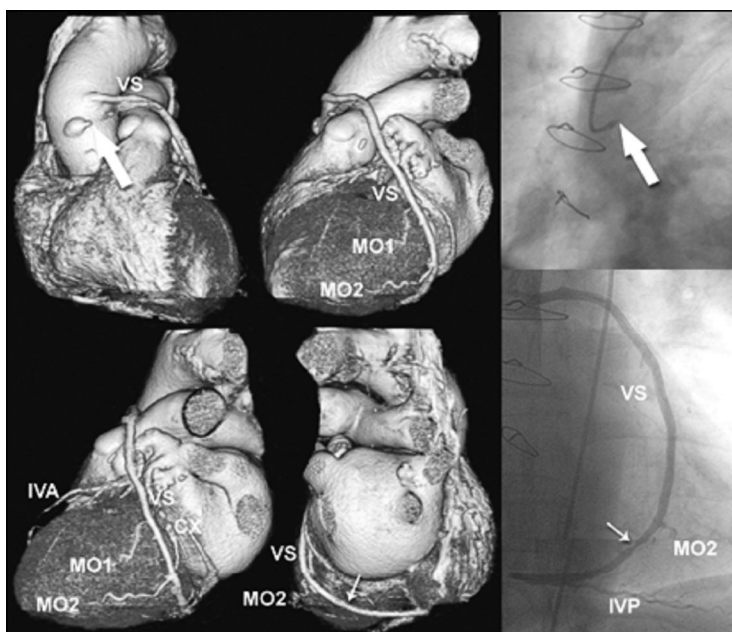
Male 58 y.o., hypercholesterolemia, diabetes, obesità, referred to exertional stable angina. Dubious exercise test, negative SPECT. MDCT-CA shows significant (>50%) Left Main stenosis ( fig. below).



**Case II.** Significant Left Main disease

### Case III

Male 73 y.o., referred for exertional angina; in 1993 two venous sequential bypass for multisegmental occlusive disease: 1, first obtuse marginal branch (1<sup>st</sup> OM ) – second obtuse marginal branch (2<sup>nd</sup> OM) – posterior descending artery (PDA); 2, Descending Anterior (DA) - second obtuse marginal branch (2<sup>nd</sup> OM). MDCT-CA shows proximal occlusion of SV-DA-2<sup>nd</sup> OM ( thick arrows) and >50% stenosi in distal tract of SV – 1<sup>st</sup> OM – 2<sup>nd</sup> OM – PDA. (fig. below)



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